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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,431	10/08/2003	Keith A. Moore	XANO / 33	7143
26875	7590	09/13/2006	EXAMINER	
WOOD, HERRON & EVANS, LLP 2700 CAREW TOWER 441 VINE STREET CINCINNATI, OH 45202			RAMACHANDRAN, UMAMAHESWARI	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/681,431

Applicant(s)

MOORE ET AL.

Examiner

Umamaheswari Ramachandran

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

Claims 26-37 are withdrawn from further consideration as applicants had elected claims 1-25 drawn to a method of treatment. Election was made **without** traverse in the reply filed on 8/4/2006. Thus the restriction requirement elected is made final.

#### ***Claim Rejections - 35 USC § 112(1)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1 and 8 are attributed to a therapeutic method of administering to a patient N-desmethyl levomepromazine (NDM LMP) does not reasonably provided enablement for the method. The specification does not provide any examples or case studies to describe the method of administering NDM LMP to a patient.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**(1) The nature of the Invention:**

All of the rejected claims are drawn to a method comprising administering to a patient NDM LMP in a pharmaceutically acceptable formulation for providing antagonist effects for dopamine, histamine, serotonin,  $\alpha$ -adrenergic, sodium ion and calcium ion channel receptors.

**(2) Breadth of the claims:**

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a therapeutic method of administering to a patient NDM LMP to provide antagonist effects to such a variety of receptors and would thus expect to affect the functions regulated by these receptors.

**(3) Guidance of the Specification:**

The guidance given by the specification for a therapeutic method comprising administering NDM LMP to a patient to provide various antagonist effects is none. All of the guidance provided by the specification is directed towards the in vitro receptor binding studies and not in vivo.

**(4) Working Examples:**

The specification provides examples for the in vitro receptor binding studies to determine the binding effect of the parent compound Levomepromazine (LMP), NDM

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LMP and the sulfoxide metabolite against various receptors. Also, the metabolism of the parent LMP to the NDM LMP and sulfoxide metabolites in vivo is discussed in the specification.

**(5) The relative skill of those in the art:**

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

**(6) The predictability of art:**

Despite the advanced training in the medical treatment arts, the arts are highly unpredictable. The state of the art is such that it is not possible to predict the activity of a compound, whether in vitro or in vivo, based on the structure alone. In order to predict the in vivo activity of a compound based on the in vitro assay, the assay itself must be definitively well correlated to the pathophysiology of a target disease and verified as being predictive of the in vivo activity of a compound. For example, if a receptor is known to be overactivated in the pathophysiology of a disease, the ordinary practitioner would predict that a compound that inhibits the activation of the receptor may be useful for the treatment of said disease. However, even for in vitro models that involve receptors known to be involved in the pathophysiology of a disease, translating the in vitro efficacy of the compound to in vivo efficacy for the treatment of a disease is notoriously unpredictable unless the correlation has been conclusively verified. Further, the in vivo efficacy of a compound is not only determined by the affinity or activity of the compound on its target receptor in a validated in vitro assay, but by a range of other

factors including the bioavailability of the compound, its pharmacokinetic profile, and the specificity of the compound for the desired target versus other potential targets.

**(7) The Quantity of Experimentation Necessary:**

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system for the claimed compound. One would then need to test the compound in the model system to determine whether or not the compound provides antagonist effects towards the various receptors. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the therapeutic method of administering to a patient the compound, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. In order to practice the applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of receptor. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of therapeutic method of administering NDM LMP to a patient to provide antagonist effects to various receptors.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, a therapeutic method for administering NDM LMP to a patient for providing antagonist effects for dopamine, histamine, serotonin,  $\alpha$ -adrenergic, sodium ion and calcium ion channel receptors of the claims is not considered to be enabled by the instant specification.

***Claim Rejections - 35 USC § 112(2)***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 6, 8, 9, 10, 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 5 and 8, line 2, the term substantial is a relative term and it is not clear of how much steady state concentration is substantial. In claim 8 the term substantial is vague and indefinite and it is not clear what applicant means in producing substantially the same pharmaceutical effects. Claim 9 is rejected as it depends on claim 8. It is not clear in claim 6 what the relatively lower dose (line 2) of NDM LMP to achieve effects like antiemetic or relatively higher dose (line 3) or a dose higher than the lower dose and lower than the higher dose as an analgesic (lines 4-5) means in terms of percentage.

**Conclusion**

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone

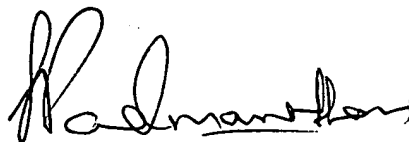
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number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SUPERVISORY PATENT EXAMINER